Current Clinical and Medical Education

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DOI: https://doi.org/10.15678/3--3-1
Curr Clin Med Educ 3 (3), 159—166 (2025)
Received 3 July 2025 | **Revised** 9 Aug 2025 | **Accepted** 14 Sep 2025 | **Online Available** 30 Sep 2025

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OPEN ACCESS

ISSN (O) 3023-3593 | (Print: 3023-3585)

ORIGINAL RESEARCH ARTICLE

To find correlation of Thwaites' and Lancet scoring systems with the microbiological diagnosis of TBM

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Abstract

Background: Tuberculous meningitis (TBM) is a severe form of extrapulmonary tuberculosis, causing significant global mortality and morbidity. Its diagnosis is challenging due to non-specific clinical presentation and limitations of conventional microbiological methods, highlighting the need for rapid diagnostic tools. **Aim:** This study aimed to correlate TBM diagnoses from the Thwaites' and Lancet clinical scoring systems with microbiological confirmation, and to assess their utility in differentiating TBM from other sub-acute and chronic meningitis etiologies. **Methods:** A cross-sectional study at SRMS-IMS, Bareilly, India, included 180 adult patients with suspected meningitis with CSF abnormalities. Patients underwent clinical evaluation using both Thwaites' and Lancet scoring systems. CSF samples were analyzed for TLC, protein, glucose, ADA, AFB/Gram stain, and rapid MGIT culture. Radiological investigations (chest X-ray, brain CT/MRI) were also performed. Statistical analysis used Mann-Whitney Test and Point-Biserial correlation. **Results:** The cohort was predominantly female (55%) and aged 21-30 (28.33%), with common complaints being fever (93.33%) and headache (83.33%). All patients showed abnormal CSF (lymphocytic predominance, low glucose, high protein), but Gram stain and AFB smears were consistently negative. Rapid MGIT culture was positive in only 11.67% (21/180) cases. Thwaites' system diagnosed all 180 patients as TBM (mean score -2.85 ± 2.51). Lancet system classified most as possible TBM (85.00%) and 11.67% as definite TBM. A significant positive correlation was found between MGIT culture positivity and the Lancet system (r=0.424, p=0.001), but not with Thwaites' system (r=0.082, p=0.531). **Conclusion:** Early diagnosis of TBM requires integrating clinical assessment, CSF findings, imaging, and diagnostic scores. Although microbiological culture remains the gold standard, its low yield highlights the importance of clinical judgment and scoring tools. The Lancet scoring system demonstrated better correlation with microbiological confirmation and supports timely initiation of ATT based on combined clinical and investigative evidence

Key words: Tuberculous Meningitis (TBM, Thwaites' Scoring System, Lancet Consensus Criteria, MGIT Culture

1 | INTRODUCTION

Meningitis is classified as acute, subacute, or chronic based on symptom duration (1) . Subacute meningitis (SAM) typically evolves over 5–30 days, while chronic meningitis (CM) exceeds 30 days with persistent CSF abnormalities (2) .

Tuberculosis remains a global health crisis, with tuberculous meningitis (TBM)—its most severe extrapulmonary form—affecting ~100,000 cases annually (1) . TBM carries high mortality and mor-

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bidity, particularly in developing nations like India, China, and Vietnam, where it ranks second in prevalence worldwide (2) . It is the second most common cause of community-acquired meningitis (3) , often presenting subacutely with diverse neurologic features, including meningoencephalitis, myelitis, cranial neuropathies, radiculopathy, paraplegia, depression, abscesses, and stroke (4, 5) ,.

Risk factors include alcoholism, diabetes, and cell-mediated immunodeficiency (e.g., HIV, immunosuppression), though it can occur in immunocompetent hosts; corticosteroids, chronic hepatitis, and cirrhosis also contribute (2, 6) .

Classic symptoms—fever, headache, stiff neck—may be absent early, with illness spanning days to months before seeking care[3]. TBM triggers inflammation leading to complications like cerebrovascular disease, cranial nerve palsies, hydrocephalus, and infarction. Prompt diagnosis and treatment are crucial to mitigate mortality and sequelae.

Diagnosis is challenging due to nonspecific presentation; differentials encompass fungal/bacterial/viral CNS infections, noninfectious meningitides (e.g., SLE), and malignancies (4)

CSF examination is crucial for TBM diagnosis, with microbial isolation via culture as the gold standard (7) . TB PCR sensitivity is 77.7% (8) , but cultures delay results (days-weeks). Empirical antibiotics are common in community-acquired meningitis (9) , once CSF culture found negative than switching to TBM therapy is challenging due to low test sensitivities. WHO recommends Xpert MTB/RIF as initial test over microscopy/culture (10) , as Indian guidelines note TBM as ~1% of TB cases (11) . Very few Indian studies use Thwaites (4) and Lancet[5] scoring systems to prevent diagnostic delays. This study correlates these scores with labs to enable early TBM treatment and differentiate from other subacute/chronic meningitides.

Scoring Systems

Two primary clinical diagnostic scoring systems, Thwaites' and the Lancet consensus system, are utilized to aid in the diagnosis and empirical treatment of TBM.

Thwaites diagnostic scoring system (4) (anexure 1) includes 5 independent parameters: age, peripheral white blood cell count, history of illness, total WBC count in CSF, and neutrophil ratio in CSF. Assign +2 points if age ≥36 years (0 if <36), +4 if blood white cell count ≥15,000/mL (0 if <15,000), -5 if duration of illness ≥6 days (0 if <6), +3 if CSF total white cell count ≥900/mL (0 if <900), and +4 if CSF neutrophil percentage ≥75% (0 if <75).The total diagnostic index (DI) was calculated for each patient according to different prefixed cut-off values. Patients with total DI values of <4 were diagnosed with TBM and those with values >4 with TBM.

Thwaites' scoring: 95.6% sensitivity, 70.8% specificity for TBM vs. bacterial meningitis[12]; microbiologically proven: 91.7%, 79.7%; AUC-ROC 0.92. Helpful for differential, but needs validation for viral meningitis/low CSF glucose. Less effective vs. partially treated bacterial[16] or HIV+ adults (12)

Lancet consensus scoring system (5)-(anexure 2)this is more precise becauseit involves various other factors and is able to define the cases based on TBM including definite, probable and possible

criteria

Clinical Criteria (maximum score 6): Assign 4 points if symptom duration exceeds 5 days, 2 points if symptoms are indicative of tuberculosis (one or more), 2 points if there is a history of recent contact with pulmonary tuberculosis or a positive tuberculin skin test or interferon-gamma release assay, 1 point if there is focal neurological deficit excluding cranial nerve deficit, 1 point if cranial nerve palsy is present, and 1 point if consciousness is altered.

CSF Criteria (maximum score 4): Assign 1 point if cerebrospinal fluid appearance is clear, 1 point if cell count is 10–500 per microliter, 1 point if there is lymphocytic predominance, 1 point if protein concentration exceeds 1 g/L, and 1 point if glucose concentration is less than 2.2 mmol/L.

Cerebral Imaging Criteria (maximum score 6): Assign 1 point if hydrocephalus is present, 2 points if basal meningeal enhancement is seen, 2 points if tuberculoma is identified, 1 point if infarct is present, and 2 points if precontrast basal hyperdensity is noted.

Evidence of TB Elsewhere (maximum score 4): Assign 2 points if chest radiograph suggests active tuberculosis, 4 points if it suggests miliary tuberculosis, 2 points if CT, MRI, or ultrasound shows tuberculosis outside the central nervous system, 4

points if acid-fast bacilli are identified or Mycobacterium tuberculosis is cultured from another source such as sputum, lymph node, gastric washing, urine, or blood, and 4 points if a positive commercial Mycobacterium tuberculosis nucleic acid amplification test is obtained from an extra-neural specimen.

Diagnosis based on total score:

1.Definite TBM: Clinical criteria + positive microbiological/histological evidence.

2. Possible TBM: score of 12 points if image available(if imaging not availability than 10).

3. Probable TBM: score of 6-11 points if image avail (if no imaging availability tha 6-9).sible, based on the scoring.

A study on the diagnostic utility of "Thwaites' system", and the "lancet consensus scoring-system" in tuberculous versus non-tuberculous sub-acute, and the chronic meningitis was performed (13) . Both criteria were easily able to differentiate TBM from bacterial meningitis; only the Lancet score was capable of differentiating TBM from viral, fungal, and unknown etiologies, even though a significant overlap occurred between etiologies (P< 0.001). Both the criteria displayed poor accuracy to differentiate TBM from the non-TBM etiologies (i.e., AUC-ROC<.5), but the Lancet scoring system of consensus was fair in identifying TBM (AUC-ROC=0.738).

STUDY DESIGN : Cross sectional study

SAMPLE SIZE :all patient suspected as meningitis in 4 year.

INCLUSION CRITERIA :Age >18yearsAll patients with clinical features suggestive of meningitisBiochemical evidence (CSF protein, sugar, TLC, DLC) suggestive of TBM

EXCLUSION CRITERIA Age < 18 yearsPatients already taking anti-tubercular therapy for > 1 month for TBMKnown cases of pyogenic meningitis, fungal meningitisCases of intracranial infection secondary to CNS surgery in last 6 weeksCases of subarachnoid hemorrhage

STATISTICAL ANALYSIS Data normality is assessed using tests like the **Kolmogorov-Smirnov test**. If data are not normally distributed, non-parametric tests are used.

The **Mann-Whitney Test** is used to analyze the association between non-normally distributed quantitative variables.

The **Point-Biserial** correlation coefficient can be used to correlate culture results with the Thwaites and Lancet scoring systems.A P-value of less than 0.05 is considered statistically significant by using software SPSS.

2 | RESULT

Study Cohort Characteristics In a cohort of 180 patients, the mean age was 39.43 ± 16.9 years with a median of 35 years (IQR 25–55 years), the largest group being 21–30 years (28.33%), and females comprising 55% compared to 45% males.

Presenting Complaints Fever was reported in 93.33% of patients, followed by headache in 83.33%, vomiting in 63.33%, altered sensorium in 56.67%, seizures in 13.33%, and hemiparesis or facial deviation in 13.33%.

Past Medical History Diabetes mellitus was present in 21.67% of patients, hypertension in 18.33%, prior tuberculosis in 13.33%, chronic kidney disease in 6.67%, and history of seizures in 14%.

Routine Laboratory Investigations Mean hemoglobin was 11.81 ± 1.69 g/dL, total leukocyte count was 9775.33 ± 5121.46 cells/mm^3, platelet count was 2.28 ± 0.85 lakh/mm^3, serum urea was 44.27 ± 51.99 mg/dL, and serum creatinine was 1.06 ± 1.56 mg/dL, with most values within normal limits.

CT/MRI Findings Hydrocephalus was observed in 24.44% of patients, vasculitis infarct in 13.33%, other abnormalities (e.g., atrophy, ischemia, old hemorrhage) in 13.33%, meningeal enhancement in 5.00%, and no significant abnormality in 43.33%.

CSF Analysis All 180 patients showed abnormal CSF with lymphocytic pleocytosis (5–900 cells/mm^3)as shown in Table 1 , elevated protein (mean 152.48 ± 92.82 mg/dL; range 22–415), low glucose (mean 40.18 ± 25.1 mg/dL; range 3–109), ADA levels ranging from 2–58 IU/L, negative Gram stain and AFB smears in all cases, and positive rapid MGIT culture in 11.67% (21 cases).

Correlation of Thwaites' and Lancet scoring systems

Table 1. CSF findings

CSFprotein(g/dL)	
Mean ± SD	152.48 ± 92.82
Median(25th-75th percentile)	141(81.5-184.75)
Range	22-415
CSFsugar(mg/dL)	
Mean ± SD	40.18 ± 25.1
Median(25th-75th percentile)	39.5(19-58.25)
Range	3-109
Corresponding blood sugar(mg/dL)	
Range	35-270
ADA(IU/L)	
Range	2-58

Diagnostic Scoring Outcomes

The Thwaites' scoring system, which incorporates patient age, duration of illness, blood TLC, CSF TLC, and CSF neutrophil percentage (with a score 1 as shown in Table 2

The Lancet consensus scoring system, which categorizes cases into definite, probable, and possible TBM based on clinical criteria, CSF criteria, cerebral imaging criteria, and evidence of TB elsewhere, classified the majority of patients as possible TBM (153 patients, 85.00%). Definite TBM was diagnosed in 21 patients (11.67%), while probable TBM was diagnosed in only 6 out of 180 patients (3.33%). As shown in Figure 1 The mean Lancet score for the study subjects was 9.02 ± 1.84, with a median (25th-75th percentile) of 9 (8-10).1

Table 2. Distribution of diagnostic score of study subjects. 1

Diagnostic score	Frequency	Percentage
Thwaites		
TBM	180	100%
Mean ± SD	-2.85 ± 2.51	
Lancet		
Definite TBM	21	11.6%
Possible TBM	153	85%
Probable TBM	6	3.33%
Mean ± SD	9.02 ± 1.84	
Range	6-15	

Correlation of Scoring Systems with MGIT Culture

Using the Point-Biserial correlation coefficient, a non-significant mild positive correlation was observed between MGIT culture results and diagnosis of TBM by the Thwaites' scoring system (correlation coefficient = 0.082, p=0.531) as shown in Table 3 . The median Thwaites' score for negative MGIT cultures was -3 (-5 to -1), and for positive MGIT cultures, it was -5 (-5 to 0), indicating no significant association (p-value = 0.971).1

In contrast, a significant positive correlation was found between MGIT culture results and the clinical diagnosis of TBM by the Lancet scoring system (correlation coefficient = 0.424, p=0.001). The median Lancet score for positive MGIT cultures was 11 (10-12.5), as shown in Figure 2 which was significantly higher compared to negative MGIT cultures (9 (8-9)) (p-value = 0.001).1

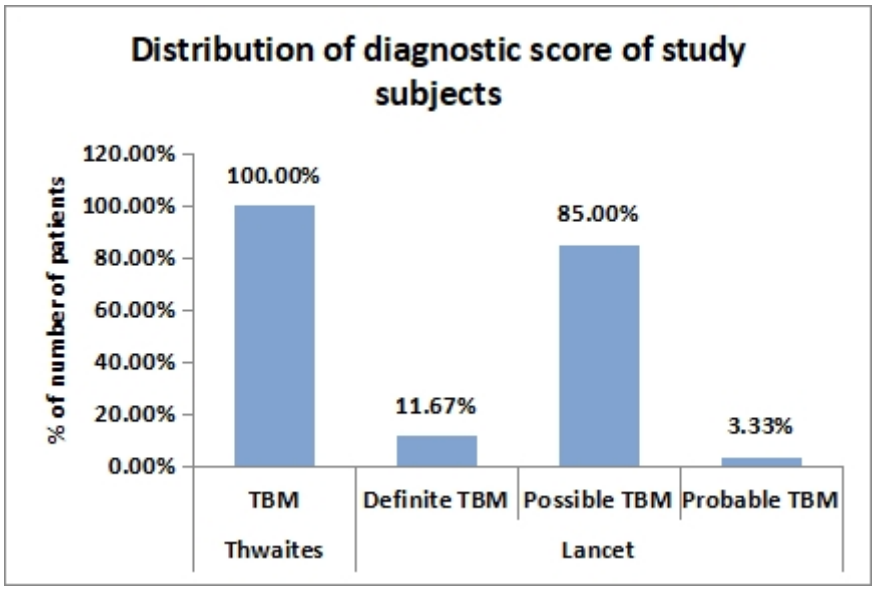

Fig. 1: Figure 1 distribution of diagnostic score of study subjects

Table 3. Correlation of MGIT culture with Thwaites and Lancet scoring. 1

Variables	Thwaites	Lancet
MGIT Culture		
Correlation coefficient	0.082	0.424
P value	0.531	0.001

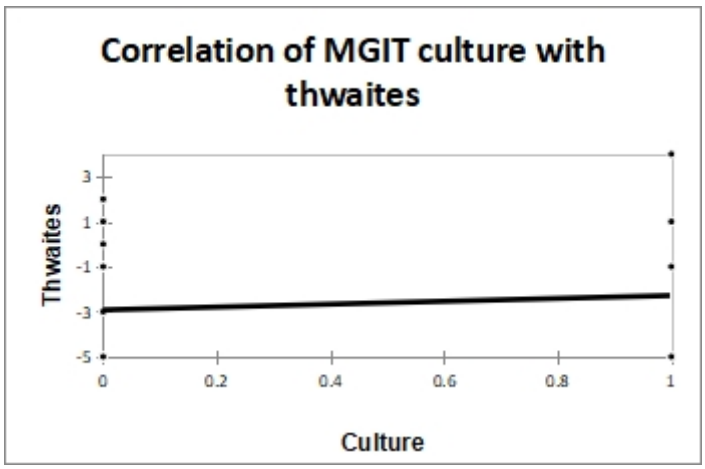

Fig. 2: correlation of MGIT culture with thwaites

• Mann Whitney test

Median of thwaites scoring in negative culture was -3(-5–1) and positive culture was -5(-5-0) with no significant association between them. (p value=0.971)

Median of lancet scoring in positive culture was 11(10-12.5) which was significantly higher as compared to negative culture (9(8-9)). (p value=0.001) as shown in Figure 3

Correlation of Thwaites' and Lancet scoring systems

Table 4. Association of diagnostic score with MGIT culture. 1

Diagnostic score	Negative Culture (n=159)	Positive Culture (n=21)	Total	P value
LANCET				
Mean ± SD	8.74 ± 1.69	11.14 ± 1.57	9.02 ± 1.84	0.001*
Median(25th-75th percentile)	9(8-9)	11(10-12.5)	9(8-10)	
Range	6-15	9-13	6-15	
THWAITES				
Mean ± SD	-2.92 ± 2.35	-2.29 ± 3.68	-2.85 ± 2.51	0.971*
Median(25th-75th percentile)	-3(-5--1)	-5(-5-0)	-3(-5--1)	
Range	-5-2	-5-4	-5-4	

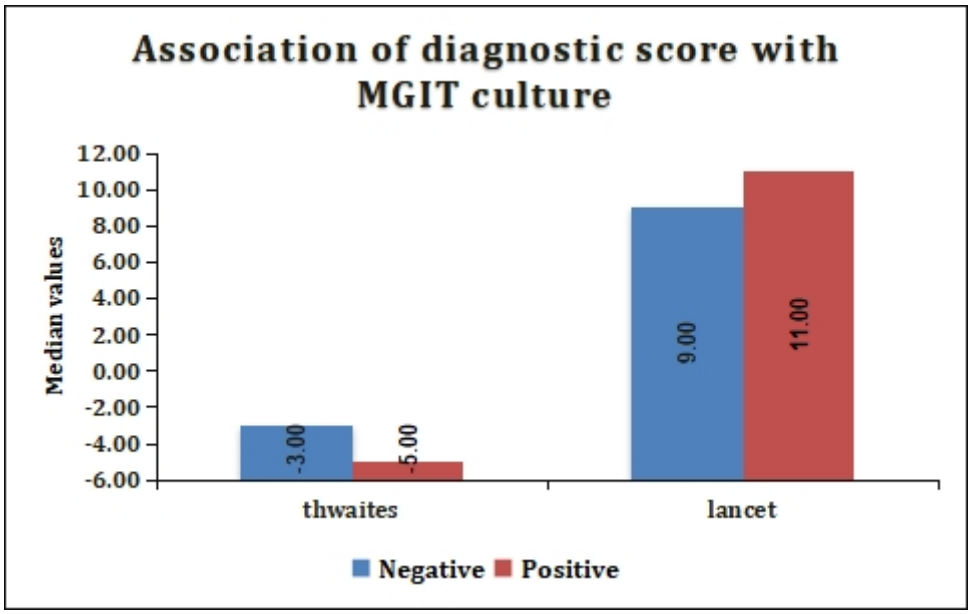

Fig. 3: -Association of diagnostic score with MGIT culture (non-parametric variable)

3 | DISCUSSION

The current study's findings align with existing literature, confirming TBM's subacute/chronic presentation with neurological symptoms like meningitis and cranial nerve involvement (14, 15) . Basal meningeal involvement often causes cranial nerve paresis, focal ischemia, hydrocephalus, and intracranial hypertension.

A notable finding was the low MGIT culture positivity (11.67%), highlighting persistent microbiological confirmation challenges and the need for empirical treatment on strong suspicion (1) .

Diagnostic Utility of Thwaites' and Lancet Scoring Systems

In 180 suspected TBM patients, Thwaites' diagnosed all as TBM but showed non-significant MGIT correlation (r=0.082, p=0.531) (1) This indicates high sensitivity for suspicion but limited specificity for confirmation, consistent with Sebastian et al. (sensitive but non-specific in HIV-negative; low accuracy in HIV-positive)[1] and Zhang et al. (less effective vs. partially treated bacterial meningitis) (1) . Thus, Thwaites' aids initial risk stratification and empirical therapy in resource-limited settings, not precise etiology.

Lancet categorized 85% (153 patients) as possible TBM and 11.67% (21) as definite[1], with significant MGIT correlation (r=0.424, p=0.001) (1) . Its integration of clinical, CSF, imaging, and extraneural TB criteria enables better differentiation from non-TBM etiologies. Sulaiman et al. corroborated this: both systems differentiate from bacterial meningitis, but only Lancet from viral/fungal/unknown (P<0.001), despite overlaps (1) .

Comparison with Existing Literature

Thwaites' echoes Sunbul et al. (95.6% sensitivity/70.8% specificity vs. bacterial) (1) ; Zhang et al. (98.2%/43.6% initial bacterial; 98.2%/24.2%

partially treated)[1]; Sebastian et al. (n=527: sensitive/non-specific in HIV-negative; low in HIV-positive)[1].

Sulaiman et al. (2020, n=395) affirmed Lancet's superiority in broader differentiation, with fair TBM accuracy (AUC-ROC=0.738; sensitivity 50%, specificity 89.3%) (1) . Lancet's parameters provide nuanced reliability across meningitides.

Overall Implications for Diagnosis and Management

Early TBM diagnosis demands integrated clinical, CSF, and imaging assessments (1) . Thwaites' and Lancet guide empirical ATT, with response validating diagnosis[1]. Despite low culture yields, empirical therapy is essential; Lancet's correlation supports its role in "possible/probable" cases

4 | CONCLUSION

This study underscores that the early diagnosis of tuberculous meningitis (TBM) necessitates a comprehensive assessment integrating clinical findings, cerebrospinal fluid (CSF) analysis, and/or radio imaging. Clinical diagnostic scores, particularly the Thwaites' and Lancet systems, are invaluable tools for guiding the timely initiation of anti-tubercular therapy (ATT).

While microbiological culture remains the gold standard, its consistently low positivity rate means a negative result does not definitively rule out TBM, especially with strong clinical suspicion. In such cases, empirical ATT is often imperative.

A non-significant correlation was observed between MGIT culture and the Thwaites' scoring system, suggesting its primary role in raising clinical suspicion. In contrast, the Lancet scoring system showed a significant positive correlation with MGIT culture. The study highlights that even cases categorized as "possible" or "probable (16) TBM by the Lancet system warrant ATT initiation and vigilant monitoring.

Given the challenges of microbiological confirmation and the severe consequences of delayed treatment, a pragmatic, risk-based approach to TBM management is crucial. This approach relies on integrating clinical suspicion, validated scoring systems, and the patient's response to empirical therapy, particularly in settings where definitive laboratory results are delayed or negative. Ultimately, the decision to initiate ATT is founded upon a comprehensive evaluation of all available investigations combined with clinical judgment.

ETHICAL CLEARANCE

This study will be carried out after approval from ethical committee of the institute.

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How to cite this article: Rawal D., Kumar S., Agrawal S., Kumar A., Tyagi A., Johri S. To find correlation of Thwaites' and Lancet scoring systems with the microbiological diagnosis of TBM. Current Clinical and Medical Education. 2025;159−166. https://doi.org/10.15678/3–3-1

Anexure 1

VARIABLE	SCORE
AGE (YEARS) • >=36 • <36	 +2 0
BLOOD WHITE CELL COUNT (10*3/mL) • >=15000 • <15000	 +4 0
DURATION OF ILLNESS (DAYS) • >=6 • <6	 -5 0
CSF TOTAL WHITE CELL COUNT (10*3/mL) • >=900 • <900	 +3 0
CSF PERCENTAGE NEUTROPHILS • >=75 • <75	+4 0

Anexure 2

S.NO.	CRITERIA	SCORE
1	CLINICAL CRITERIA	(MAX. SCORE=6)
	Symptom duration >5 days	4
	Symptoms indicative of TB (one, or more)	2
	H/o recent contact with pulmonary TB or positive TST or IGRA	2
	The focal neurological deficit (excluding the cranial nerve deficit)	1
	Cranial nerve palsy-	1
	Altered consciousness	1
2	CSF CRITERIA	(MAX. SCORE=4)
	Clear appearance-	1

	Cells 10-500/microlitre	1
	Lymphocytic predominance	1
	Protein concentration >1g/l	1
	CSF glucose concentration <2.2mmol/l	1
3	CEREBRAL IMAGING CRITERIA:	(MAX. SCORE=6.)
	Hydrocephalus:	1
	The basal meningeal enhancement:	2
	Tuberculoma:	2
	Infarct	1
	Precontrast basal hyperdensity	2
4	EVIDENCE OF THE TB ELSEWHERE	(MAX. SCORE=4)
	Chest radiograph suggestive of- Active TB Miliary TB	 2 4
	CT/MRI/USG evidence for TB outside CNS	2
	AFB identified, or M.Tuberculosis cultured from another source-sputum, lymph node, gastric washing, urine, blood culture	4
	Positive commercial M.Tuberculosis NAAT from extra-neural specimen	4